

Attorney Docket No. 9368-6IP

Cofe

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Olmsted et al.

U.S. Patent No.: 6,783,939 B2

Application Serial No.: 09/991,258

Issued: August 31, 2004

Filed: November 16, 2001

For: *Alphavirus Vectors and Virosomes with Modified HIV Genes for Use in Vaccines*

Date: December 3, 2004

Commissioner for Patents

Attn: Certificate of Correction Branch

P.O. Box 1450

Alexandria, VA 22313-1450

Certificate
DEC 20 2004
of Correction

**REQUEST FOR ENTRY OF CERTIFICATE OF CORRECTION UNDER
35 U.S.C §254 AND 37 C.F.R. §1.322**

Sir:

The Assignee of record for the above-referenced patent hereby requests, pursuant to 35 U.S.C §254 and 37 C.F.R. §1.322, that a Certificate of Correction be issued. This request is made in order to correct the mistakes incurred through the fault of the U.S. Patent and Trademark Office. No fee is believed due. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

The mistakes appearing in the patent are set forth with corrections on the Certificate of Correction enclosed herewith, with an additional copy thereof and a return post card.

Respectfully submitted,

Mary L. Miller

Registration No. 39,303

Myers Bigel Sibley & Sajovec, P.A.

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Monica L. Croom

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,783,939 *B2*
DATED : August 31, 2004
INVENTOR(S) : Olmsted et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

Column 167, claim 1 should read -- 1. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Column 167, claim 2 should read -- 2. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- 3. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- 7. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 8 should read -- 8. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing

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an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 9 should read -- 9. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 169, claim 13 should read -- 13. An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Columns 169-170, claim 18 should read -- 18. A method of making the alphavirus replicon particle of claim 17, comprising

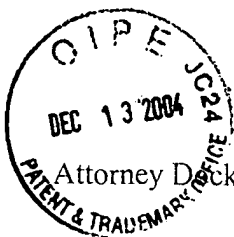
- a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:
 - (i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;
 - (ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and
 - (iii) one or more additional helper RNA(s) separate from said replicon RNA and separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;
- and with at least one of said helper RNAs lacking an alphavirus packaging signal;
- wherein the combined expression of the alphavirus replicon RNA and the helper RNAs produces an assembled alphavirus replicon particle which is able to infect a cell, and is unable to complete viral propagation, and further wherein the population contains no detectable replication-competent alphavirus particles as determined by passage on permissive cells in culture;
- (b) producing the alphavirus replicon particles in the helper cell; and
- (c) collecting the alphavirus replicon particles from the helper cell. --

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DEC 20 2004



Attorney Docket No. 9368-61P

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Column 167, claim 2 should read -- 2. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- 3. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- 7. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

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Column 169, claim 13 should read -- **13.** An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Columns 169-170, claim 18 should read -- **18.** A method of making the alphavirus replicon particle of claim 17, comprising

- a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:
 - (i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;
 - (ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and
 - (iii) one or more additional helper RNA(s) separate from said replicon RNA and separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;
- and with at least one of said helper RNAs lacking an alphavirus packaging signal;
- wherein the combined expression of the alphavirus replicon RNA and the helper RNAs produces an assembled alphavirus replicon particle which is able to infect a cell, and is unable to complete viral propagation, and further wherein the population contains no detectable replication-competent alphavirus particles as determined by passage on permissive cells in culture;
- (b) producing the alphavirus replicon particles in the helper cell; and
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